

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P02/087-bzgs	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 03/ 06055	International filing date (day/month/year) 10/06/2003	(Earliest) Priority Date (day/month/year) 11/06/2002
Applicant MERCK PATENT GMBH		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

MODIFIED BYRODIN 1 WITH REDUCED IMMUNOGENICITY

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Publication No

PCT/EP 03/06055

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K47/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBL, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 34317 A (ADAIR FIONA SUZANNE ;CARR FRANCIS JOSEPH (GB); HAMILTON ANITA ANNE) 15 June 2000 (2000-06-15) cited in the application the whole document See especially Example 4 and Figure 10 ---	1-16
A	WO 98 52976 A (BIOVATION LTD ;CARR FRANCIS J (GB)) 26 November 1998 (1998-11-26) ---	
A	ALTUVIA Y ET AL: "RANKING POTENTIAL BINDING PEPTIDES TO MHC MOLECULES BY A COMPUTATIONAL THREADING APPROACH" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 249, no. 1, 1995, pages 244-250, XP000925520 ISSN: 0022-2836 --- -/--	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

6 October 2003

Date of mailing of the international search report

23/10/2003

Name and mailing address of the ISA

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Turri, M

INTERNATIONAL SEARCH REPORT

International Publication No
PCT/EP 95/06055

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SPENCER D I R ET AL: "A STRATEGY FOR MAPPING AND NEUTRALIZING CONFORMATIONAL IMMUNOGENIC SITES ON PROTEIN THERAPEUTICS" PROTEOMICS, XX, XX, vol. 2, no. 3, March 2002 (2002-03), pages 271-279; XP009009265 ---	
A	MEISTER G E ET AL: "Two novel T cell epitope prediction algorithms based on MHC-binding motifs; comparison of predicted and published epitopes from Mycobacterium tuberculosis and HIV protein sequences" VACCINE, BUTTERWORTH SCIENTIFIC, GUILDFORD, GB, vol. 13, no. 6, 1 April 1995 (1995-04-01), pages 581-591, XP004057605 ISSN: 0264-410X ---	
A	WEBER J R ET AL: "IMMUNODOMINANT STRUCTURES OF HUMAN GROWTH HORMONE IDENTIFIED BY HOMOLOG-SCANNING MUTAGENESIS" MOLECULAR IMMUNOLOGY, ELMSFORD, NY, US, vol. 29, no. 9, 1992, pages 1081-1088, XP009004807 ISSN: 0161-5890 ---	
A	MOOLA Z B ET AL: "ERWINIA CHRYSANTHEMI L-ASPARAGINASE: EPI TOPE MAPPING AND PRODUCTION OF ANTIGENICALLY MODIFIED ENZYMES" BIOCHEMICAL JOURNAL, PORTLAND PRESS, LONDON, GB, vol. 302, no. PART 3, 1994, pages 921-927, XP000918634 ISSN: 0264-6021 ---	
A	CUNNINGHAM B C ET AL: "HIGH-RESOLUTION EPI TOPE MAPPING OF HGH-RECEPTOR INTERACTIONS BY ALANINE-SCANNING MUTAGENESIS" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, US, vol. 244, no. 4908, 2 June 1989 (1989-06-02), pages 1081-1085, XP000025308 ISSN: 0036-8075 ---	
A	SALI A ET AL: "COMPARATIVE PROTEIN MODELLING BY SATISFACTION OF SPATIAL RESTRAINTS" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 234, 1993, pages 779-815, XP002948615 ISSN: 0022-2836 ---	
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INTERNATIONAL SEARCH REPORT

International Publication No

PCT/EP 03/06055

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>KWOK W W ET AL: "Rapid epitope identification from complex class-II-restricted T-cell antigens" TRENDS IN IMMUNOLOGY, ELSEVIER, CAMBRIDGE, GB, vol. 22, no. 11, 1 November 2001 (2001-11-01), pages 583-588, XP004319746 ISSN: 1471-4906</p> <p>---</p>	
T	<p>WO 02 069232 A (MERCK PATENT GMBH ; CARTER GRAHAM (GB); JONES TIM (GB); CARR FRANCI) 6 September 2002 (2002-09-06)</p> <p>---</p>	
A	<p>GAWLAK SUSAN L ET AL: "Molecular, biological, and preliminary structural analysis of recombinant bryodin 1, a ribosome-inactivating protein from the plant Bryonia dioica." BIOCHEMISTRY, vol. 36, no. 11, 1997, pages 3095-3103, XP002256641 ISSN: 0006-2960 cited in the application -& DATABASE EMBL 'Online! 21 November 2001 (2001-11-21) GAWLAK, S L. ET AL.: "Ribosome-inactivating protein 'Bryonia dioica!" retrieved from EMBL Database accession no. AAL34334 XP002256642 the whole document</p> <p>---</p>	
A	<p>US 5 541 110 A (SIEGALL CLAY B) 30 July 1996 (1996-07-30) cited in the application</p> <p>---</p>	
A	<p>STIRPE F ET AL: "BRYODIN A RIBOSOME-INACTIVATING PROTEIN FROM THE ROOTS OF BRYONIA-DIOICA L. WHITE BRYONY" BIOCHEMICAL JOURNAL, vol. 240, no. 3, 1986, pages 659-666, XP009018531 ISSN: 0264-6021</p> <p>---</p>	
A	<p>BATTELLI M G ET AL: "TOXICITY OF AND HISTOLOGICAL LESIONS CAUSED BY RIBOSOME-INACTIVATING PROTEINS THEIR IGG-CONJUGATES AND THEIR HOMOPOLYMERS" APMIS, vol. 98, no. 7, 1990, pages 585-593, XP009018529 ISSN: 0903-4641</p> <p>---</p>	
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INTERNATIONAL SEARCH REPORT

International Publication No

PCT/EP 03/06055

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>FRYXELL DANIEL K ET AL: "Identification of a specific tyrosine residue in Bryodin 1 distinct from the active site but required for full catalytic and cytotoxic activity"</p> <p>PROTEIN SCIENCE, vol. 7, no. 2, February 1998 (1998-02), pages 318-324, XP009018559 ISSN: 0961-8368</p> <p>-----</p>	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claim : 14 and 15

A peptide part of Bryodin 1 comprising one or more T-cell epitopes.

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/EP 03/06055

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/06055

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0034317	A	15-06-2000	AU 1667600 A	26-06-2000
			CA 2342967 A1	15-06-2000
			CN 1294596 T	09-05-2001
			EP 1051432 A2	15-11-2000
			WO 0034317 A2	15-06-2000
			JP 2002534959 T	22-10-2002
			AU 4635699 A	24-01-2000
WO 9852976	A	26-11-1998	AU 736549 B2	02-08-2001
			AU 7539398 A	11-12-1998
			EP 0983303 A1	08-03-2000
			WO 9852976 A1	26-11-1998
			GB 2339430 A	26-01-2000
			JP 2002512624 T	23-04-2002
			US 2003153043 A1	14-08-2003
WO 02069232	A	06-09-2002	WO 02062832 A2	15-08-2002
			WO 02062375 A1	15-08-2002
			WO 02077034 A2	03-10-2002
			WO 02062843 A2	15-08-2002
			WO 02062842 A1	15-08-2002
			WO 02062833 A2	15-08-2002
			WO 02066058 A1	29-08-2002
			WO 02069232 A2	06-09-2002
US 5541110	A	30-07-1996	AT 245697 T	15-08-2003
			CA 2148724 A1	18-11-1995
			DE 69531332 D1	28-08-2003
			EP 0710723 A1	08-05-1996
			JP 8098694 A	16-04-1996
			US 5932447 A	03-08-1999